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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/703,253	10/31/2000	Marrie Harras	LEX-0081-USA	1776

7590 07/09/2002

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EXAMINER
LANDSMAN, ROBERT S

ART UNIT	PAPER NUMBER
1647	14

DATE MAILED: 07/09/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/703,253	Applicant(s) HARRAS ET AL.	
	Examiner Robert Landsman	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4/23/02* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4* is/are pending in the application.

4a) Of the above claim(s) *3-4* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence Comparisons A-D* .

DETAILED ACTION

1. Formal Matters

A. Amendment A, filed 4/23/02, has been entered into the record. Claims 1-4 are pending in the application. Applicants have stated on page 3 of the "Response" dated 4/23/02 that claims 3 and 4 have been cancelled as being drawn to a non-elected invention. However, there were no instructions to do so in the "Amendment" section of the Response. Therefore, claims 1-4 remain pending and claims 1 and 2 are the subject of this Office Action.

Applicants traversed the restriction requirement in the Office Action of Paper No. 11, dated 12/19/01. Applicants argue that the nucleic acid sequence described in SEQ ID NOs:23 and 1 (and the amino acid sequences they encode, 24 and 2, respectively) are all encoded by a common genetic locus and are splice variants. Therefore, Applicants argue that Groups I and II should have been combined. This argument has been considered, but not deemed persuasive. Though SEQ ID NO:1 and 23 may be encoded by a common genetic locus, they are still independent and distinct, each from each other, because they are products which possess characteristic differences in structure and function and each has an independent utility that is distinct for each invention which cannot be exchanged. Therefore, they would require individual searches of the sequence databases and a search of one sequence would not necessarily uncover art on the other sequence. Therefore, this restriction is deemed proper and is made FINAL.

DJK

B. The syntax of claim 1 could be improved by replacing the phrase "first disclosed in the NHP gene described in" with "of."

C. The syntax of claim 2 could be improved by replacing the phrase "shown in" with "of."

D. All Statues under 35 USC not found in this Office Action can be found, cited in full, in a previous Office Action.

2. Oath/Declaration

A. The objection to the Declaration has been withdrawn since Applicants have provided a new Declaration in which the changes to the residence of Gregory Donoho have been initialed.

3. Title

A. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The present title is "Novel human transporter proteins and polynucleotides encoding the same." First, the word "novel" should be omitted from the title, since all patents contain novel subject matter. Second, the claims are drawn toward polynucleotides encoding

human transporter proteins and not to the proteins themselves. Therefore, the title should be amended to, for example, "Polynucleotides encoding human transporter proteins."

4. Specification

A. The specification is objected to since the Abstract is not concise. Applicant is reminded of the proper content of an abstract of the disclosure.

A patent abstract is a concise statement of the technical disclosure of the patent and should include that which is new in the art to which the invention pertains. If the patent is of a basic nature, the entire technical disclosure may be new in the art, and the abstract should be directed to the entire disclosure. If the patent is in the nature of an improvement in an old apparatus, process, product, or composition, the abstract should include the technical disclosure of the improvement. In certain patents, particularly those for compounds and compositions, wherein the process for making and/or the use thereof are not obvious, the abstract should set forth a process for making and/or use thereof. If the new technical disclosure involves modifications or alternatives, the abstract should mention by way of example the preferred modification or alternative.

The abstract should not refer to purported merits or speculative applications of the invention and should not compare the invention with the prior art.

Where applicable, the abstract should include the following:
(1) if a machine or apparatus, its organization and operation;
(2) if an article, its method of making;
(3) if a chemical compound, its identity and use;
(4) if a mixture, its ingredients;
(5) if a process, the steps.

Extensive mechanical and design details of apparatus should not be given.

5. Claim Rejections - 35 USC § 101

A. Claims 1 and 2 remain rejected under 35 USC 101, for the reasons already of record on pages 3-6 of the Office Action dated 12/19/01. Applicants argue that it is clear that the nucleic acid sequences of the present invention, and the amino acid sequences which they encode, are novel transporters involved in multiple drug resistance (MDR) and belong to the ABC superfamily of transporters. They argue that a "specific and substantial utility" has been asserted and that these proteins have been characterized, in part, by their ability to mediate the passage of materials across the lipid bilayer as well as in multiple drug resistance. However, as discussed below, these arguments do not demonstrate a "specific or substantial utility" for the claimed nucleic acid molecules, or encoded proteins.

Applicants provide GENBANK Accession Nos. AY040219 (Tammur et al.) and AF367202 (Yabuuchi et al.) and argue that these nucleic acid sequences encoding ABC transporters both have 99% identity to SEQ ID NO:23 of the present invention. Applicants state that AY040219 has a total of 4145 of 4149 bases which are similar to those of SEQ ID NO:23 of the present invention, and that AF367202 has a total of 4141 of 4149 bases which are similar to those of SEQ ID NO:23.

First, it is noted that the Applicants have stated that SEQ ID NO:23 is 4149 bases in length. However, the Paper Copy of the Sequence Listing in the specification shows that SEQ ID NO:23 is only 3660 bases in length. Furthermore, a search of these Accession Nos. against SEQ ID NO:23 of the present invention shows that, in fact, the nucleotide sequences are not each 99% identical to SEQ ID NO:23, but only 86% identical (Sequence Comparisons A and B). The polynucleotides of Tammur et al. and Yabuuchi et al. both have an additional 488 bases not found in SEQ ID NO:23. Therefore, the polynucleotide of SEQ ID NO:23 is "lacking" a large (13% of the entire polynucleotide structure) section of the polynucleotides of Tammur et al. and Yabuuchi et al. As seen on pages 5-6 of the Office Action dated 12/19/01, the art acknowledges that function cannot be predicted based solely on structural similarity to a protein. The same, therefore, is true regarding the polynucleotides encoding these proteins. Therefore, based on these teachings in the art, it would not be expected that a polynucleotide "lacking" 488 bases of sequences as compared to a similar polynucleotide would have the same function, or encode a protein with the same function, as that in the art. While Applicants argue that these and other post-filing papers provided in the Response of 4/23/02 teach a well-established and substantial utility of ABC transporters in drug resistance, Applicants have not established that it is more likely than not that the nucleic acid molecules of the present invention do, in fact, encode MDRs, so the relevance of ABC transporters (which includes the MDRs) cannot be extrapolated to the present invention.

Furthermore, the utility of ABC transporters is to transport various compounds, or families of compounds, from cells. As seen in the post-filing paper of Tammur et al. (Abstract; Gene 273:89-96, 2001), the ABC superfamily of transporters is currently comprised of three different transporter types, the MDR-like, sulfonylurea receptor, and CFTR gene and the phylogenetic analysis of these transporters further divides these transporters into seven subfamilies (first paragraph of the Introduction, page 89). In fact, Tammur et al. teach that their MDR gene (ABCC11), which Applicants argue is similar to SEQ ID NO:23 of the present invention, is most similar to ABCC5 (page 94, left column, second full paragraph) and that ABCC5 confers resistence to PMEA (page 93, right column, first paragraph). However, Tammur et al. teach that no difference was seen in expression levels of ABCC11 between the parental and PMEA-resistant cell lines, demonstrating that even though ABCC11 is closely related to ABCC5, the function of

ABCC11 cannot be predicted based on the function of ABCC5. Therefore, in addition to the polynucleotides of the present invention only showing 86% identity to those of Tammur et al. and Yabuuchi et al., Applicants have also not identified which types, or families, of drugs are transported by the proteins of the present invention, as this cannot be predicted by sequence homology to known ABC transporters, further making the present invention incomplete.

Applicants further argue that there is an entire industry based on the use of gene sequences, or fragments thereof, in gene chip format, and even in non-gene chip format. Applicants argue that the existence and acquisition of companies in this industry, as well as projects such as the Human Genome Project, demonstrate a substantial utility which is well-established. Applicants argue that the present nucleotide sequences clearly encode a novel human transporter and, therefore, that the present sequences are specific markers of the human genome which are targets for the discovery of drugs that are associated with human disease, and that even "negative information" has a great "real-world" practical utility. Again, based on the discussion in the above paragraphs, it is not clear that the nucleotides of the present invention encode a human transporter. Furthermore, the specification does not disclose any function, nor any dysfunction, associated with altered levels or forms of the nucleic acid molecules of the present invention. Significant further experimentation would be required of the skilled artisan to identify a dysfunction or disease associated with the claimed nucleic acid molecules. There is no disclosure, for example, of any symptoms associated with such a disease or dysfunction of these nucleic acid molecules. Additionally, the use of the nucleic acid molecules of the present invention in gene chip, or non-gene chip technologies, or to analyze gene expression is not a specific or substantial utility since any nucleic acid molecule can be used for this purpose. In addition, the tissues shown to express these nucleic acid molecules have not been shown to be specific for the nucleic acid molecules of the present invention. Finally, the argument that the presently described cDNAs provide biologically validated empirical data is also not persuasive since this is not a specific utility of this cDNA compared to the thousands of DNA molecules that encode thousands of potentially unrelated proteins. It is believed that all pertinent arguments have been addressed.

6. Claim Rejections - 35 USC § 112, first paragraph - enablement

A. Claims 1 and 2 remain rejected under 35 USC 112, first paragraph, for the reasons already of record on page 6 of the Office Action dated 12/19/01 as well as for the reasons given in the above rejection under 35 USC 101. Applicants argue that the claimed invention is enabled because it has utility as argued previously. Applicants' arguments have been fully considered, but are not found to be persuasive for the reasons discussed above.

B. Claims 1 and 2 remain rejected under 35 USC 112, first paragraph, regarding "hybridization" and "at least 24 contiguous bases of SEQ ID NO:23." The Examiner inadvertently did not include claim 1 as a rejected claim number in the first sentence of the rejection on page 7 of the Office Action, dated 12/19/01 and Applicants did not address this issue. However, it should be clear that the rejection included claim 1 since the body of the rejection recites "at least 24 contiguous bases of SEQ ID NO:23," which only appears in claim 1. Regardless, Applicants' arguments regarding "hybridize" are deemed persuasive only if the nucleic acid molecule of the present invention were shown to have utility. However, since Applicants have not demonstrated utility of the nucleic acid molecule of SEQ ID NO:23 under 35 USC 101, then this enablement rejection regarding (a) a nucleic acid molecule which hybridizes to SEQ ID NO:23 and encodes SEQ ID NO:24, or (b) which comprises at least 24 contiguous bases of SEQ ID NO:23, stands.

7. Claim Rejections - 35 USC § 112, first paragraph – written description

A. The rejection of claims 1 and 2 under 35 USC 112, first paragraph, regarding "hybridize" and "at least 24 contiguous bases of SEQ ID NO:23" has been withdrawn in view of Applicants' arguments that the specification does adequately describe the claimed nucleic acid molecules. The Examiner inadvertently did not recite which claims were subject of this rejection on page 8 of the Office Action dated 12/19/01. This rejection was intended to cover claims 1 and 2. Regardless, the rejection under 35 USC 112, first paragraph, has been withdrawn.

8. Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

A. Claim 2 remains rejected under 35 USC 112, second paragraph, regarding "stringent conditions" for the reasons already of record on pages 9-10 of the Office Action dated 12/19/01. Applicants have amended the claim to recite "highly stringent conditions." However, the metes and bounds of this phrase are not known. It is suggested that part (b) of claim 2 be deleted since this limits the scope of the claim. If Applicants wish to keep part (b) in the claim, they should amend the claim to recite the exact hybridization conditions as found, for example, on page 4, lines 7-11 of the specification.

B. Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is not clear if the "complement thereof" in part (b) is the complement of the claimed nucleic acid molecule, or if the claimed nucleic acid molecule hybridizes to the complement of SEQ ID NO:23.

9. Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

A. The rejection of claim 1 under 35 USC 102(b) as being anticipated by Suzuki et al. has been withdrawn since the molecule of Suzuki et al. may hybridize to SEQ ID NO:23, but does not encode SEQ ID NO:24, as required by part (a) of claim 2. This rejection was initially intended to be made over claim 2, and not claim 1. Regardless, the rejection has been withdrawn.

B. Claim 1 is rejected under 35 U.S.C. 102(a) as being anticipated by Mahairas et al. The claim recites an isolated nucleic acid molecule comprising at least 24 contiguous bases of SEQ ID NO:23. Mahairas et al. (Proc. Natl. Acad. Sci. USA 96:9739-9744, 1999 – Sequence Comparison C) teach a nucleic acid molecule which is 162 contiguous bases of SEQ ID NO:23.

C. Claim 1 is rejected under 35 U.S.C. 102(a) as being anticipated by Adams et al. The claim recites an isolated nucleic acid molecule comprising at least 24 contiguous bases of SEQ ID NO:23. Adams et al. (Accession No. - April 08, 1999 – Sequence Comparison D) teach a nucleic acid molecule which is 68 contiguous bases of SEQ ID NO:23.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
July 01, 2002